Complete Summary

GUIDELINE TITLE

Obstetric cholestasis.

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). Obstetric cholestasis. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Jan. 10 p. (Guideline; no. 43). [61 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Obstetric cholestasis (previously referred to as intrahepatic cholestasis of pregnancy)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To summarise the evidence for the fetal risks associated with obstetric cholestasis and to provide guidance on the different management choices and the options available for its treatment

TARGET POPULATION

Women with diagnosed or suspected obstetric cholestasis

INTERVENTIONS AND PRACTICES CONSIDERED

1. Liver function tests
    - Transaminases
    - Gamma glutamyl transferase
    - Bilirubin and/or bile salts
2. Assessment of signs and symptoms
3. Physical examination
4. Screening for hepatitis A, B, and C virus; Epstein Barr virus, chronic active hepatitis, and primary biliary cirrhosis
5. Liver ultrasound
6. Risk assessment for and advising women concerning fetal and maternal complications
7. Vitamin K supplements

Note: The following interventions and practices are considered but not recommended: fetal monitoring for the prediction of fetal death, fetal ultrasound for preventing fetal death, elective early delivery, topical emollients, S-adenosyl methionine (SAMe), ursodeoxycholic acid, dexamethasone.

MAJOR OUTCOMES CONSIDERED

- Maternal morbidity
- Fetal risks (including prematurity and intrauterine death)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Cochrane Library, Issue 4, 2003, Medline from 1966 to November 2003, and Embase from 1980 to week 46, 2003, were searched for English language papers only, using the following keywords: cholestasis; cholestasis intrahepatic; ursodeoxycholic acid; s-adenosylmethionine; rifampin; rifampicin; histamin h1 antagonists; antihistaminic agent; chlorpheniramine; cholestyramine; colestyramine; vitamin K; vitamin K group; bile pigments; pruritus; itch; liver; bilirubin; bile; transaminases; pregnancy; pregnancy complications; dexamethasone; betamethasone; congenital, hereditary and neonatal diseases and abnormalities; embryo and fetal development; neurons; developmental disabilities; infant low birth weight; newborn disease; prenatal disorder; nervous system development; developmental disorder; liver function tests; bile acids and salts; aminotransferase pregnancy; pregnancy complications; risk; fetus risk; risk factors; recurrent disease; recurrence; incidence; morbidity; mortality; fetal death; prevalence; familial incidence; heredity; genetics; diagnosis, and the subheadings; diagnosis; epidemiology; morbidity; genetics.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well-designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The recommendations were graded according to the level of evidence upon which they were based. The grading scheme used was based on a scheme formulated by the Clinical Outcomes Group of the National Health Service (NHS) Executive.

Grade A - Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia, Ib)

Grade B - Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendations (evidence levels IIa, IIb, III)

Grade C - Requires evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV)

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Following discussion in the Guidelines and Audit Committee, each green-top guideline is formally peer reviewed. At the same time the draft guideline is published on the Royal College of Obstetricians and Gynaecologists (RCOG) Web site for further peer discussion before final publication.

The names of author(s) and nominated peer reviewers are included in the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.

Levels of evidence (Ia-IV) and grading of recommendations (A-C) are defined at the end of the "Major Recommendations" field.

How is Obstetric Cholestasis Diagnosed?

C - Pregnancy-specific reference ranges for liver function tests (LFTs) should be used.

C - Other causes of itching and of liver dysfunction should be excluded.

C - Postnatal resolution of pruritus and LFTs should be confirmed.

In obstetric cholestasis, the pruritus is typically worse at night, is often widespread, and may involve the palms of the hands or the soles of the feet. Other causes of pruritus must be excluded. The skin should be inspected and care must be taken to differentiate dermatographia artefacta (skin trauma from intense scratching), which may be seen in obstetric cholestasis, from other common skin conditions such as eczema and pruritic eruption of pregnancy. Other evidence of cholestasis should be sought, including pale stool, dark urine, and family history of obstetric cholestasis.

In clinical practice, abnormalities in transaminases, gamma glutamyl transferase, bilirubin, and/or bile salts are considered sufficient to support the diagnosis of obstetric cholestasis.

If, in routine practice, bile salt assessment is not easily available, it would be reasonable, at present, only to obtain levels in women with pruritus who have persistently normal LFTs.

Other causes of abnormal LFTs should be excluded. A viral screen for hepatitis A, B, and C, Epstein Barr, and cytomegalovirus, a liver autoimmune screen for chronic active hepatitis and primary biliary cirrhosis (for example, anti-smooth muscle and antimitochondrial antibodies), and liver ultrasound should be carried out before the diagnosis is confirmed.

How Should Obstetric Cholestasis be Monitored?

C - Once obstetric cholestasis is diagnosed, it is reasonable to measure LFTs weekly.

C - Postnatal LFTs should be deferred for at least 10 days.

What is the Risk of Stillbirth for Pregnancies Complicated by Obstetric Cholestasis?

B - Obstetricians should be aware (and should advise women) that the current stillbirth rate for obstetric cholestasis is comparable to that in the general population. The risk of stillbirth in "untreated" obstetric cholestasis is unclear.

What Additional Risks are Associated with Pregnancies Complicated by Obstetric Cholestasis?

B - Obstetricians should be aware (and should advise women) that the incidence of premature birth is increased, both spontaneous and iatrogenic.

B - Obstetricians should be aware (and should advise women) that the evidence for an increased risk of meconium-stained liquor, caesarean section, or postpartum haemorrhage is inconclusive.

Can Fetal Death be Predicted and Prevented?

B - Delivery decisions should not be based on the degree of abnormality of biochemical tests, as current data are not robust enough to demonstrate or exclude a correlation between maternal levels of liver enzymes or bile salts and intrauterine death.

C - No specific fetal monitoring modality for the prediction of fetal death can be recommended.

B - Ultrasound is not a reliable method for preventing fetal death in obstetric cholestasis.

Should Women with Obstetric Cholestasis be Offered Elective Early Delivery?

B - Obstetricians should be aware that there are insufficient data to support or refute the popular practice of "early" (37 weeks of gestation) induction of labour aimed at reducing late stillbirth.

What Treatment, if any, Should be Used to Treat Obstetric Cholestasis and What Benefit Can be Expected?

There is no evidence that any specific treatment improves maternal symptoms or neonatal outcomes. All such therapies should be discussed with the individual woman with this in mind.

Topical Emollients

C - Topical emollients are safe but their efficacy is unknown.

S-Adenosyl Methionine

A - There is insufficient evidence to show whether S adenosyl methionine is effective for either control of maternal symptoms or for improving fetal outcome.

Ursodeoxycholic acid

A - There are insufficient data to support the widespread use of ursodeoxycholic acid (UDCA) outside of clinical trials. Women should be aware of the lack of robust data concerning improvement in pruritus, protection against stillbirth, and safety to the fetus or neonate.

Dexamethasone

B - Dexamethasone should not be first-line therapy for obstetric cholestasis, nor should it be used outside of a randomised controlled trial (RCT) without a thorough consultation with the woman.

What is the Role of Vitamin K?

C - It is reasonable to offer a daily supplement of water-soluble vitamin K to all women from diagnosis of obstetric cholestasis. If there is frank steatorrhoea or prolongation of the prothrombin time, the clinical case for the use of vitamin K is stronger.

What Follow-up Should be Offered to Women Who Have Had a Pregnancy Affected by Obstetric Cholestasis?

As a minimum, healthcare practitioners must ensure that LFTs return to normal, pruritus resolves, all investigations carried out during the pregnancy have been reviewed, and the mother had fully understood the implications of obstetric cholestasis. The latter will include reassurance about the lack of long-term sequelae for mother and baby, the high recurrence rate, discussion of contraceptive choices (usually avoiding oestrogen-containing methods), and the increased incidence of obstetric cholestasis in family members. Local policy will dictate how this is best organised.

Definitions:

Grading of Recommendations

Grade A - Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence levels Ia, Ib)

Grade B - Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendations (evidence levels IIa, IIb, III)

Grade C - Requires evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV)

Levels of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well-designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, and case studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of obstetric cholestasis to improve maternal and fetal outcomes

POTENTIAL HARMS

None stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Clinical guidelines are "systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions." Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: Guidance for the Development of Royal

College of Obstetricians & Gynaecologists (RCOG) Green-top Guidelines. (See the "Availability of Companion Documents" field in this summary.)

- These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources, and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.
- The wide range of definitions of obstetric cholestasis and the absence of agreed diagnostic criteria make comparisons of the published literature challenging and limit the ability to provide detailed recommendations for specific aspects of care.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Royal College of Obstetricians and Gynaecologists (RCOG). Obstetric cholestasis. London (UK): Royal College of Obstetricians and Gynaecologists (RCOG); 2006 Jan. 10 p. (Guideline; no. 43). [61 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Jan

GUIDELINE DEVELOPER(S)

Royal College of Obstetricians and Gynaecologists - Medical Specialty Society

SOURCE(S) OF FUNDING

Royal College of Obstetricians and Gynaecologists

GUIDELINE COMMITTEE

Guidelines and Audit Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor Deirdre J Murphy, MRCOG (Chair); Caroline Bearfield, Guidelines Research Fellow; Ms Toni Belfield, Consumers' Representative; Professor P R Braude, FRCOG, Chairman, Scientific Advisory Committee; Mrs C Dhillon, Head of Clinical Governance and Standards Dept.; Dr Martin Dougherty, A. Director NCC-WCH; Miss L M M Duley, FRCOG, Chairman, Patient Information Subgroup; Mr Alan S Evans, FRCOG; Dr Mehmet R Gazvani, MRCOG; Dr Rhona G Hughes, FRCOG; Mr Anthony J Kelly MRCOG; Dr Gwyneth Lewis, FRCOG, Department of Health; Dr Mary A C Macintosh, MRCOG, CEMACH; Dr Tahir A Mahmood, FRCOG; Mrs Caroline E Overton, MRCOG, Reproductive medicine; Dr David Parkin, FRCOG; Oncology; Ms Wendy Riches, NICE; Mr Mark C Slack, MRCOG, Urogynaecology; Mr Stephen A Walkinshaw, FRCOG, Maternal and Fetal Medicine; Dr Eleni Mavrides, Trainees Representative

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Guideline authors are required to complete a "declaration of interests" form.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.

Print copies: Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Bookshop, 27 Sussex Place, Regent's Park, London NW1 4RG; Telephone: +44 020 7772 6276; Fax, +44 020 7772 5991; e-mail: bookshop@rcog.org.uk. A listing and order form are available from the RCOG Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Guidance for the development of RCOG green-top guidelines. Clinical Governance Advice No 1. 2000 Jan. Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.
- Searching for evidence. Clinical Governance Advice No 3. 2001 Oct. Available from the Royal College of Obstetricians and Gynaecologists (RCOG) Web site.

Additionally, audit criteria can be found in section 14 of the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 10, 2006. The information was verified by the guideline developer on April 26, 2006.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/25/2006